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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,310	03/14/2001	Samir Khleif	15280415100	9099
20350	7590	07/27/2005		
TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			EXAMINER DIBRINO, MARIANNE NMN	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/810,310

Applicant(s)

KHLEIF ET AL.

Examiner

DiBrino Marianne

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,6-8 and 11-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-8 and 11-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

S.O.D

### DETAILED ACTION

1. Applicants' amendment filed 5/23/05 is acknowledged and has been entered.

**The following are new grounds of rejection necessitated by Applicant's amendment filed 5/23/05.**

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to elicit an immune response in a subject comprising administering *in vivo* a peptide or protein antigen from an HIV protein comprising one or more T cell epitopes with a non-viral vector comprising a polynucleotide encoding at least one of a B7-1, B7-2 or B7-3 co-stimulatory molecule recited in the instant claims. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a method of eliciting an immune response that will treat or prevent HIV.

The specification discloses that a secondary "co-stimulation" signal is required for optimal stimulation and effective antigen specific clonal expansion of lymphocytes in addition to a primary antigen specific signal, and that a two signal model has been proposed for all lymphocytes (page 3 at lines 14-19). The specification discloses that the primary activation signal typically involves an antigenic peptide bound to either class I or class II MHC (page 3 at lines 20-22). The specification discloses that T cell co-stimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and is thought to involve binding of co-stimulatory molecules on the surface of APC to a corresponding T cell ligand (page 3 at lines 30-33 and continuing on to page 4 at lines 1-10). The specification discloses that B7 is one co-stimulatory molecule for T cells and is a counter receptor for CD28 and CTLA-4 (page 4 at lines 11-23), and that two additional receptors related to B7 (B7-1), are B7-2 and B7-3 (page 5 at lines 5-8). The specification further discloses along with B7-1, B7-2, B7-3, that B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 are co-stimulatory molecules (especially page 7 at lines 17 and 18). The specification discloses immunizing mice with a peptide antigen emulsion, i.e., an HPV E7 peptide, followed by an intradermal injection of B7-encoding DNA plasmid vector (especially Example 1). The specification further discloses measuring CTL extracted, i.e., *ex vivo*, from the said mice for immunoreactivity to the E7 immunizing peptide and an increased effect when B7-

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encoding DNA plasmid vector was coordinately administered with the peptide antigen. The instant specification does not disclose treatment of subjects with peptide antigens other than the aforementioned HPV E7 peptide antigen and a non-viral vector encoding a co-stimulatory molecule other than B7.1. The specification does not exemplify treatment or prophylaxis of HIV infection *in vivo* by injecting a B7-1, -2 or -3-encoding DNA or RNA plasmid vector and HIV antigen in the method recited in the instant claims.

Evidentiary reference PROMT Accession No. 1998: 555242 (Lancet 24 Oct. 1998, pp 1323(1), of record) teaches virus variability is an important problem facing HIV vaccine researchers, that researchers have very little idea about what constitutes protective immunity, which animal model is best suited to test vaccine candidates, and that the gap between a vaccine candidate and product development remains vast. The said reference further teaches that ethical concerns surrounding clinical trials have yet to be resolved.

Evidentiary reference U.S. Patent No. 5,942,607 (of record) discloses that in AIDS (i.e., HIV infection), viral replication is stimulated by T cell activation, and that blocking of B7-2 and possibly also B7-1 and B7-3 will ameliorate the course of AIDS by slowing down the growth of HTLV-1 (HIV)-induced leukemias (especially column 18 at lines 23-34).

Evidentiary reference Letvin (of record) teaches that virus-specific antibody response does not play a critical role in either the chronic or early containment of HIV replication in the infected individual (page 16, column 1, last sentence of the first full paragraph), that the neutralization-sensitive domains of the virus have proven poorly immunogenic (second to last line of the next paragraph on page 16 at column 1) and that HIV appears to be controlled predominantly by cell-mediated immunity (page 16 at column 1, last paragraph). Letvin also teaches that the immunopathogenesis of AIDS suggests that HIV is unique in its biology and may therefore not be amenable to control by immune responses elicited through traditional vaccine modalities (page 16 at paragraph 2, column 2).

There is insufficient guidance in the specification as to how to practice the method of the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments of record in the amendment filed 5/23/05 have been fully considered, but are not persuasive.

Applicant's arguments are of record on pages 6-10 of the said amendment at the section titled "Enablement", briefly that (1) therapeutic or pharmacological inventions satisfy utility under 35 USC 101 and therefore, under the "how to use" requirement under 35 USC 112 where "any benefit" is provided to the public, (2) that discovery of the physiological effect of administering a peptide or protein antigen coordinately with a non-viral vector encoding at least one of B7-1, B7-2 or B7-3 to provide an enhanced

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immune response provides an "immediate benefit" to the public, (3) the claims do not themselves recite enhancement or supplementation of an immune response "to a clinical isolate replicating *in vivo*", (4) that eliciting an immune response to an antigen comprising one or more T cell epitopes even in the absence of a corresponding clinical isolate replicating *in vivo* in a subject could be used to potentiate a prophylactic effect against a pathogenic agent comprising the one or more T cell epitopes whether or not the subject ever actually encounters a pathogenic agent comprising the particular epitopes.

It is the Examiner's position that the disclosed used for the claimed method is to vaccinate and treat (especially page 6 at lines 1-6). It is the Examiner's further position that the instant specification does not exemplify, nor does the admitted prior art disclosed in the instant specification, *in vivo* treatment or prophylaxis of any animal using an HIV protein or peptide antigen. In addition, evidentiary reference U.S. Patent No. 5,942,607 discloses that in HIV infection viral replication is stimulated by T cell activation, and that blocking of B7-2 and possibly also B7-1 and B7-3 will ameliorate the course of AIDS by slowing down the growth of HTLV-1 (HIV)-induced leukemias, *i.e.*, teaching away from stimulating T cells in HIV infected patients. Furthermore, evidentiary reference PROMT Accession No. 1998: 555242 (Lancet 24 Oct. 1998, pp 1323(1)) teaches virus variability is an important problem facing HIV vaccine researchers, that researchers have very little idea about what constitutes protective immunity, which animal model is best suited to test vaccine candidates, and that the gap between a vaccine candidate and product development remains vast, and ethical concerns surrounding clinical trials have yet to be resolved. And evidentiary reference Letvin et al teach that the immunopathogenesis of AIDS suggests that HIV is unique in its biology and may therefore not be amenable to control by immune responses elicited through traditional vaccine modalities.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,942,607 (IDS reference) in view of Kaufmann et al (Cell. Immunol. 1996, 169/2 246-251, of record), admitted prior art in the specification on page 37 at lines 7-18, Rock et al (PNAS USA 89: 8918-8922, 1992, IDS reference), U.S. Patent No. 5,738,852 (of record), WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of WO 98/04705 (both of record), U.S. Patent No. 6,338,947 and U.S. Patent No. 6,045,802.

During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification." Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. In re Prater 162 USPQ 541, 550 - 51 (CCPA 1969).

The limitation "closely adjacent" can be broadly interpreted to read on sites of undetermined distance since they can be functionally closely adjacent as disclosed in the instant specification on page 42 at lines 21-32, *i.e.*, "typically, when the peptide or protein antigen and vector are administered separately, they are delivered to the same or closely proximate site(s), for example to a single target tissue or to adjacent sites that are structurally or fluidly connected with one another (e.g., to allow direct exposure of the same cells, e.g., fluid flow transfer, dissipation or diffusion through a fluid or extracellular matrix of both vaccine targets."

U.S. Patent No. 5,942,607 discloses using nucleic acid molecules encoding B7 co-stimulatory molecules such as B7-1, B7-2 or B7-3 to enhance the immunogenicity of a mammalian cell such as an APC, by transfecting the said cells with the said nucleic acid molecules and sequentially pulsing with an appropriate peptide or protein pathogen-related antigen to enhance T cell activation and immune stimulation. U.S. Patent No. 5,942,607 discloses transfecting mammalian cells with the said nucleic acid molecule comprising a regulatory sequence *in vivo* via gene therapy techniques. U.S. Patent No. 5,942,607 discloses administering therapeutically active amounts by injection such as via subcutaneous, topical or intravenous routes. U.S. Patent No. 5,942,607 discloses use of the nucleic acid molecules encoding B7-1, B7-2 or B7-3 in anti-viral therapy to activate and generate CD8<sup>+</sup> CTL. U.S. Patent No. 5,942,607 discloses cDNA or RNA encoding B7 co-stimulatory molecules. U.S. Patent No. 5,942,607 discloses pharmaceutical carriers (especially column 3 at lines 34-60, column 8 at lines 4-17 and lines 59-67, column 15 at lines 46-62, column 18 at lines 66-67, column 19 at lines 1-18, column 20 at lines 10-33, and Abstract).

U.S. Patent No. 5,942,607 does not disclose *in vivo* administration of a *non-viral vector* comprising a nucleic acid molecule encoding a B7 co-stimulatory molecule coordinately, *i.e.*, separately and sequentially, to closely adjacent sites, with a peptide or protein antigen comprising one or more T cell epitopes, including wherein the peptide antigen comprises at least nine contiguous amino acid residues of an HPV antigenic protein.

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Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of co-stimulatory molecules such as CD80 (B7.1). Kaufman et al teach that introduction and expression of B7.1 gene in cervical carcinoma cells expressing HPV E7 renders the cells more immunogenic, that CTL induced against the said cells can lyse the parental tumor cells and that it is expected that these CTL will specifically lyse the tumor cells in vivo.

The prior art admission in the specification on page 37 at lines 7-18 is that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long-term expression of the protein encoded by the DNA. Applicant discloses the prior art references at lines 14-18. One of the said prior art references, Fynan et al teach that epidermal, mucosal, intramuscular and intravenous routes of administration can be used for DNA vaccines (especially Discussion section).

Rock et al teach that peptides of optimal length that bind to class I MHC molecules are 8-10 amino acid residues, *i.e.*, they may be CD8<sup>+</sup> CTL epitopes if they are recognized by the said CTL.

U.S. Patent No. 5,738,852 discloses inducing partial immunity by administering recombinant polynucleotides, including in the form of non-viral vectors or naked DNA or RNA operably linked to regulatory elements for expression, encoding an immunostimulatory factor such as B7.1 and/or a target antigen polypeptide from a viral protein (entire document, especially Abstract, claims, column 4 at lines 45-67, column 6 at lines 31-32, column 9 at lines 40-46, column 10 at lines 36-46, column 13 at lines 41-67, and claims). U.S. Patent No. 5,738,852 discloses administration by any suitable means known in the art including by parenteral means, *i.e.*, such as "subcutaneous" recited in instant claim 15. U.S. Patent No. 5,738,852 discloses that separate polynucleotides can encode the antigenic polypeptide and the co-stimulatory molecule, each is mixed with a suitable excipient and the number and timing of doses is determined by routine methods known to those of skill in the art. U.S. Patent No. 5,738,852 discloses that the immune response that ensues results from the expression of both polypeptides in an APC in the individual (especially abstract).

WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the WO 98/04705 document teach a pharmaceutical composition for treating a HPV infection comprising HPV E7 polypeptides and a co-stimulatory molecule B7.1 or a recombinant vector encoding the polypeptides.

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U.S. Patent No. 6,338,947 discloses that antigenic proteins or peptides for use in vaccines may be administered in combination with an appropriate adjuvant or in the form of genetic constructs. U.S. Patent No. 6,338,947 discloses that the proteins or peptides may be combined with costimulatory molecules, or adjuvants and/or carriers such as a saponin, GM-CSF, interleukin, emulsifying oils or heat shock proteins (especially column 11 at lines 25-39 and column 12 at lines 11-21).

U.S. Patent No. 6,045,802 discloses that using an admixture of vector encoding recombinant antigen and vector encoding recombinant-B7 costimulatory molecule can lead to coinfection and coexpression on APCs so as to enhance specific T cell responses, and that it is advantageous to use separate vectors so that the vector encoding B7-costimulatory molecule can be used with other antigens associated with a tumor or disease agent for enhancement of an immune response (especially Example 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the teaching of the enhancement of immune response to antigen by coordinate B7 costimulatory molecule expression as per the disclosure of U.S. Patent No. 5,942,607, Kaufman et al, U.S. Patent No. 5,738,852 and U.S. Patent No. 6,045,802 by administering the co-stimulatory molecule(s) disclosed by U.S. Patent No. 5,942,607, U.S. Patent No. 5,738,852, and taught by Kaufman et al, WO 98/04705 and CAPLUS Accession No. 1998: 106018 *in vivo* as a nucleic acid molecule as disclosed by U.S. Patent No. 5,942,607 in the form of a non-viral vector such as those taught by the prior art admitted references disclosed in the instant specification on page 37 at lines 7-18, including as taught by Fynan et al, and as disclosed by U.S. Patent No. 5,738,852, coordinately to closely adjacent sites with a polypeptide antigen(s) as disclosed by U.S. Patent No. 5,942,607 in order to "pulse" the APC with antigen as disclosed by U.S. Patent No. 5,942,607, said antigen such as the HPV E7 polypeptide taught by Kaufman et al or the pathogen-related antigen(s) disclosed by U.S. Patent No. 5,942,607, and to administer them as peptides that comprise CTL epitopes of 8-10 amino acid residues as taught by Rock et al in conjunction with adjuvants or carriers such as disclosed by U.S. Patent No. 6,338,947.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to enhance CTL response because U.S. Patent No. 5,942,607 discloses that co-stimulatory molecules can be administered *in vivo* as nucleic acid molecules that encode them in gene therapy and the APC are to be subsequently pulsed with antigen in order to enhance immune response via CD8<sup>+</sup> CTL, Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of co-stimulatory molecules such as CD80 (B7.1), and the prior art admission in the specification teaches that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA, and Fynan et al teach multiple routes of administration can be used to administer DNA vaccines,



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WO 98/04705 and the CAPLUS Accession No. 1998: 106018 teach and U.S. Patent No. 5,738,852 discloses pharmaceutical compositions comprising B7 co-stimulatory molecules or nucleic acid molecules encoding them, and U.S. Patent No. 5,738,852 discloses inducing partial immunity by administering recombinant polynucleotides, including in the form of non-viral vectors or naked DNA or RNA operably linked to regulatory elements for expression. One of ordinary skill in the art at the time the invention was made would have been motivated to do this, particularly when it was desirable to use an adjuvant with the peptide antigen(s) because U.S. Patent No. 6,338,947 discloses that antigenic proteins or peptides for use in vaccines may be administered in combination with an appropriate adjuvant or in the form of genetic constructs and that the proteins or peptides may be combined with costimulatory molecules, or adjuvants and/or carriers such as a saponin, GM-CSF, interleukin, emulsifying oils or heat shock proteins. In addition, one of ordinary skill in the art at the time the invention was made would have been motivated to administer the peptide antigen(s) at a closely adjacent site to the one used to inject the polynucleotide encoding the costimulatory molecule because U.S. Patent No. 5,738,852 discloses that the immune response that ensues results from the expression of both polypeptides in an APC in the individual. Additional motivation is derived from U.S. Patent No. 6,045,802 which discloses that using an admixture of vector encoding recombinant antigen and vector encoding recombinant-B7 costimulatory molecule can lead to coinfection and cospression on APCs so as to enhance specific T cell responses, i.e., injection of two the two molecules separately led to coinfection and enhanced immune response.

With regard to the inclusion of claim 8 in the instant rejection, the minimal peptide epitope that binds to an HLA class I molecule to induce a CTL response is from 8-10 amino acid residues in length as taught by Rock et al. For example, peptides that bind to a common MHC class I molecule in humans, HLA-A2.1, are of minimal length 9 amino acid residues.

Applicant's arguments in Applicant's amendment filed 5/23/05 have been fully considered, but are not persuasive.

Applicant's arguments are of record in the said amendment on pages 10-11 at the section entitled "Rejections under 35 U.S.C. 103", briefly, that it was known to those in the art from long-standing literature on transfection of cells that transfecting two vectors simultaneously typically results in uptake of both vectors or of neither vector by the same cells, but not just one; that there is no teaching or suggestion in the art that administration of vector and antigen "separately to closely adjacent sites" would accomplish the goal of achieving antigen presentation and vector expression in the same cells.

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It is the Examiner's position that U.S. Patent No. 5,942,607 discloses transfecting APC, including by *in vivo* gene therapy techniques, then pulsing the transfected APC with peptide antigen. It is the Examiner's further position as to Applicant's first presented argument, that the instant claims are not drawn to transfection of two vectors, but to administration of a vector and a peptide, and further that U.S. Patent No. 6,045,802 discloses that using an admixture of vector encoding recombinant antigen and vector encoding recombinant-B7 costimulatory molecule can lead to coinfection and cospression on APCs so as to enhance specific T cell responses, in contrast to Applicant's assertion. Applicant has made an assertion that it was known to those in the art from long-standing literature that transfection of two vectors simultaneously would either transfect the same cells or not at all, but has not presented evidence to that effect.

6. No claim is allowed.

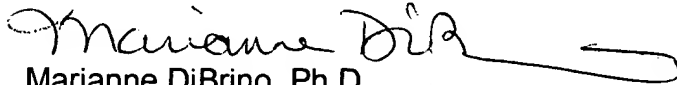
7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Marianne DiBrino, Ph.D.

Patent Examiner

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July 22, 2005



CHRISTINA CHAN

SUPERVISORY PATENT EXAMINER

TECHNOLOGY CENTER 1600